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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/670,119	06/25/1996	GORDON Y.K. NG	056365-5049	3008

7590 05/06/2004

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EXAMINER	
KUNZ, GARY L	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 05/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/670,119	NG ET AL.	
	Examiner	Art Unit	
	Gary Kunz	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *67-86* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *67-78 and 80-86* is/are rejected.

7)☒ Claim(s) *79* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *copy of specification*.

RESPONSE TO AMENDMENT

Applicant's amendment filed February 13, 2004 is acknowledged. Claims 1-66 have been canceled. Claims 67-86 are new. Claims 67-86 are pending and under consideration. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claim Rejections/Objections Withdrawn

The rejection of claims 18, 20-37 and 60-65 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention is withdrawn in response to Applicant's cancellation of these claims.

The rejection of claims 18, 20-22, 36, and 60-61 under 35 U.S.C. 102(b) as being anticipated by Lofts *et al.* is withdrawn in response to Applicant's cancellation of these claims.

The rejection of claims 18, 20-24, 26, 28-29, 36-37, and 60-61 under 35 U.S.C. 102(e) as being anticipated by Murphy *et al.* is withdrawn in response to Applicant's cancellation of these claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 67-78 and 81-86 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skill in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection. Claims 67-78 and 81-86 are drawn to

peptides comprising at least nine contiguous amino acid residues from a transmembrane domain of an alpha-1A adrenergic receptor. However, there are no examples of antagonist peptides nine amino acid residues in length. Applicants argue on p. 7 of the response that there is support using a peptide as small as 9 amino acid residues in length on p. 60 of the specification. There is no p. 60 in the specification. Looking at Applicant's other arguments, it appears that they were looking at WO 97/35881 (Ng *et al.*), a related International Publication.

Claim 80 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection. Claim 80 is drawn to a peptide comprising the sequence VFKVIFWLGYFNS and it is identified as SEQ ID NO: 32. However, SEQ ID NO: 32 identifies a tyrosine kinase receptor antagonist. The sequence VFKVIFWLGYFNS cannot be found in the specification. The peptide is considered to be new matter.

The rejection of claims 18, 20-26, 28-30, 32-33, 35-37, and 60-65 under 35 U.S.C. 112, first paragraph, for lack of enablement, is withdrawn in response to Applicant's cancellation of these claims. New claims 67-78 and 81-86 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using the defined peptide sequences listed in claims 79 and 80 that are antagonists to alpha-1A adrenergic receptors, would still not reasonably provide enablement for peptides of at least 9 amino acids of any transmembrane domain of an alpha-1A adrenergic receptor, peptides containing one or more conservative amino acid substitutions in the nine amino acids, peptides containing side chain modifications or peptides containing non-natural amino acids. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants argue on p. 7 of the response that there is support using a peptide as small as 9 amino acid residues in length on p. 60 of the specification. As stated above, there is no p. 60 in

the specification. Furthermore there are no alpha-1A adrenergic antagonist peptides that are 9 amino acid residues in length. The alpha-1A adrenergic peptide used in the working example is 16 amino acid residues in length. The other disclosed peptides are between 14 and 26 amino acid residues in length. The specification fails to disclose any peptide that is 9 amino acids in length that acts as an antagonist to an alpha-1A adrenergic receptor. In addition, the specification provides no guidance as to which (if any) of the transmembrane sequence amino acids can be changed or deleted to yield a functional equivalent of the antagonist peptide. Applicants have not provided any evidence that peptides consisting of 9 amino acids would be effective at inhibiting the activity of alpha-1A adrenergic receptors.

Applicants argue that examples of conservative amino acid substitutions are disclosed in the specification, and as such the skilled artisan could readily determine which conservative substitutions are encompassed to practice the invention without undue experimentation (p. 8 of response). The amino acid sequence of a polypeptide determines its structural and functional properties, and predictability of which amino acids can be substituted or deleted is extremely complex and well outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure from mere sequence data are limited. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, such as various sites or regions directly involved in binding, activity, and in providing the correct three-dimensional spatial orientation of binding and active sites.

Since detailed information regarding the structural and functional requirements of the peptide antagonists is lacking, it is unpredictable as to which peptides, if any, meet the limitations of the claims. Therefore it would require undue experimentation by one of skill in the art to practice the invention as claimed without further guidance from the instant specification.

The rejection of claims 18, 20-26, 28-30, 32-33, 35-37, and 60-65 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is withdrawn in response to Applicant's cancellation of these claims. New claims 67-78 and 81-86 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are drawn to a genus, *i.e.* peptide antagonists of alpha-1A adrenergic receptors. Applicants have disclosed certain peptides, SEQ ID NOS: 23-29 and 31, but have not disclosed sufficient species for the broad genus which includes any peptide comprising at least 9 contiguous amino acid residues, peptides comprising one or more conservative amino acid substitutions, peptides comprising one or more side chain modifications, and peptides comprising one or more non-naturally occurring amino acid residues.

Applicants argue that the claims meet the written description requirement because the specification provides multiple examples of peptides derived from the transmembrane domains of the alpha-1A adrenergic receptor that are effective for modulating receptor activity (p. 8 of response). Applicants further argue that according to the specification any peptides containing conservative amino acid substitutions must retain activity (p. 8 of response).

Applicant's arguments have been considered but have not been found to be persuasive. The instant disclosure of specific peptides that are antagonists to alpha-1A adrenergic receptors does not adequately describe the scope of the claimed genus, which encompasses hundreds of different peptides with varying structures and functions. While Applicants have disclosed specific peptides that can serve as antagonists to alpha-1A adrenergic receptors, they have not disclosed any positions at which mutations or modifications may have either positive, deleterious, or no affect on the binding affinity for the alpha-1A adrenergic receptors. Although Applicants argue that any modified peptide must retain activity, they have not described the genus in a way such that one of skill in the art would be able to identify effective antagonist peptides. Similarly, it is not known whether a peptide comprising 9 amino acid residues of an alpha-1A adrenergic receptor would be effective at inhibiting the activity of an alpha-1A adrenergic receptor, or whether the sequence must be at least 14 residues in length like the

peptides listed in claim 79. It is also not known what side chain modifications or amino acid substitutions would destroy the antagonistic activity of the peptides. One of skill in the art would need to first engineer the peptide and then test it for activity before establishing whether or not it was a peptide of the invention. One of skill in the art would not think from the specification that Applicants had in their possession such antagonist peptides.

Therefore, only the methods for treating disorders for which administration of a specific antagonist (a peptide selected from the group consisting of SEQ ID NOS: 23-29 and 31) of an alpha-1A adrenergic receptor, but not the full breadth of the claims, meet the written description provision of 35 U.S.C. § 112, first paragraph.

Conclusion

Claim 79 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 67-78 and 80-86 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary Kunz who can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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